Amendment

in the Specification

Please replace the title of Table 1, page 21, lines 21-24, with the following title.

Table 1

Localization Signals for Targeting to the Mitochondria.
(verified using Mitochondrial Project MITOP Database [[--]]
~~http://mips.gsf.de/proj/medgen/mitop/~~)

Please replace the paragraph beginning on page 30, line 2 with the following paragraph.

The identification of the specific sequences necessary for translocation of a linked protein into a chloroplast or mitochondria can be determined using predictive software known to those skilled in the art~~, including the tools located at http://www.mips.biochem.mpg.de/cgi-bin/proj/medgen/mitofilter~~.

Please replace the paragraph beginning on page 19, line 34 with the following paragraph.

Once inside the organelle, the nucleic acid can be integrated into the genome of the organelle. Thus, an embodiment of the present disclosure is directed to a polypeptide comprising at least a partial viral capsid protein sequence and organelle targeting sequence, for example the targeting sequences of the proteins or peptides listed in Table 1 or Table 2. The hybrid polypeptide can be expressed independently or can be expressed as part of a viral vector.

Please replace the paragraph beginning on page 21, line 5 with the following paragraph.

Organelle localization signals are known to those skilled in the art, and any of those signals can be used to target the viral vector to the target organelle. Localization sequences suitable for use in the present disclosure are described in Emanuelson et al., Predicting Subcellular Localization of Proteins Based on Their N-terminal Amino Acid Sequence. *Journal of Molecular Biology.* 300(4):1005-16, 2000 Jul 21, and in Cline and Henry, Import and Routing of Nucleus-encoded Chloroplast Proteins. *Annual Review of Cell & Developmental Biology.* 12:1-26, 1996, the disclosures of which are incorporated herein by reference in their entirety. More particularly, a list of genes and proteins with mitochondria localization signals for targeting linked proteins or nucleic acids to the mitochondria is listed in **TABLE 1.** A list of proteins, polypeptides, and nucleic acids encoding polypeptides with chloroplast localization signals for targeting linked proteins or nucleic acids to the chloroplasts is listed in **TABLE 2.** In one embodiment the mitochondria or chloroplast localization signal is operably linked to a virus surface protein. It will be appreciated that part or all of the sequences listed in Tables 1 and 2 can be used as organelle targeting sequences.

Please replace the paragraph beginning on page 31, line 12 with the following paragraph.

Another embodiment of the disclosure provides a cell having a modified organelle, wherein the modified organelle includes an exogenously introduced nucleic acid. An exogenous nucleic acid means a nucleic acid not naturally associated with the organelle or located in the organelle's interior. The nucleic acid expressed in the organelle can be transcribed and/or translated within the organelle. Additionally, the nucleic acid and its resultant protein can undergo posttranslational modification within the organelle, if necessary, to facilitate its function. Delivery of modified viral vectors to specific organelles can be accomplished using targeting sequences, for example the targeting sequences of the genes and proteins in Table 1.

Please replace the paragraph beginning on page 34, line 11 with the following paragraph.

Another embodiment provides a method for transfecting cellular organelles, for example eukaryotic organelles, by providing a virus having a targeting signal. The targeting signal can be a polypeptide, modified or unmodified, displayed on the surface of the virus which enables the virus to specifically associate with the target organelle. Exemplary targeting signals include mitochondrial targeting signals including the targeting signals of the genes and proteins listed in

TABLE 1 and other signals having a net positive charge. Contacting a cell with the recombinant vector, for example a viral vector, in a manner that introduces the vector into the cytosol of said cell as an intact functioning vector. The vector then associates with its specific target organelle and the recombinant DNA is introduced into the organelle. Introduction of the recombinant DNA into the organelle can be accomplished by transducing the vector across organelle membranes via a protein transduction domain expressed on a surface of the vector.

Please replace the paragraph beginning on page 35, line 3 with the following paragraph.

In accordance with one embodiment a method is provided for introducing exogenous nucleic acid sequences into a mitochondrion of a mammalian cell. Any mitochondrial transfection technique should ensure that a nucleic acid crosses three membranes (the plasma membrane and the outer and inner mitochondrial membranes), addresses the high copy of mtDNA molecules, and utilizes a minimal, circular mitochondrial replicon. In one embodiment of the present disclosure a recombinant bacteriophage is used as a delivery vehicle for introducing nucleic acid sequences into an organelle, for example the mitochondrion, wherein the vector does not bind to a lambda phage receptor expressed on the surface of the mitochondrion. Rather, the lambda phage vector associates with the mitochondrion via a

mitochondrial targeting sequence, for example a targeting sequence of the genes and proteins listed in Table 1.